REMARKS/ARGUMENTS

Reconsideration of this application, as amended, is respectfully requested.

The Examiner has objected to the drawings, indicating that the drawings do not have correct margins or clarity as to the invention or process depicted. The applicants have attached to this amendment replacement sheets for Figure 1 and Figure 2 prepared in accordance with 37 CFR 1.84. The attached replacement sheets are formal versions of the originally filed Figures 1 and 2 and do not contain any new matter. It is respectfully submitted that the Examiner's objection to the drawings has been obviated.

The Examiner has objected to the specification, and in particular, the Abstract. The Examiner has indicated that the abstract uses the legal phraseology, "said". The applicants have submitted on page 2 of this Amendment a replacement Abstract, in which "said" has been replaced in all instances by "the". It is respectfully submitted that the Examiner's objection to the specification has been obviated.

The applicants further note that at pages 2 – 3 of this Amendment, they have amended several additional paragraphs in order to correct minor typographical errors.

The Examiner has objected to claim 1 because of informalities, specifically the misspelling of the word "Alzheimer's," and the use of the word "and" where the word "an" should have been used. Claim 1 has been amended with the appropriate corrections made. It is respectfully submitted that the Examiner's objection to claim 1 has been obviated.

The Examiner has rejected claims 3, 4, 6, and 7 under 35 USC 112, as being indefinite for failing to point out and distinctly claim the subject matter which applicants regard as the invention.

With regard to claim 3, the Examiner has indicated that the term "specified level" in claim 3 is a relative term which renders claim 3 indefinite. The applicants have amended claim 3 to read that the process further comprises the step of measuring the level of the antagonist in the brain, rather than the step of "allowing said antagonist to reach a specified level in said patient's brain." Bases for this amendment may be found at page 13, lines 1 – 18 of the specification. It is respectfully submitted that the Examiner's rejection of claim 3 has been obviated.

With regard to claim 4, the Examiner has indicated that the term "peak level" in claim 4 is a relative term which renders claim 4 indefinite. The applicants have amended claim 4 such that the process further comprises the steps of making repeated measurements of the level of the antagonist in the brain of the patient, comparing the level obtained in the most current measurement with the level in the preceding measurement, and then administering said anticholinesterase agent to the patient when the level obtained in the most current of the repeated measurements is less than or equal to the level obtained in the measurement immediately preceding the most current of the repeated measurements. The term "peak level" in original claim 4 has thus been eliminated. It is respectfully submitted that the Examiner's rejection of claim 4 has been obviated.

With regard to claims 6 and 7, the Examiner has indicated that the term "additional amount" in claims 6 and 7 is a relative term which renders claims 6 and 7 indefinite. The applicants have amended claim 6 to read that the process further comprises the step of administering said antagonist to said patient after said step of measuring said level of said anticholinesterase in said brain of said patient. It is noted

that in amended claim 1, there is described the steps of *first* administering the antagonist, followed by the step of administering an anticholinesterase agent. Claims 3 and 5 clearly indicate the step of measuring the level of the anticholinesterase in the brain of the patient follows *first* administering the antagonist. Thus the step of adding the antagonist to the patient after the step of measuring the level of the anticholinesterase in the brain of the patient is clearly distinct from the step of first administering the antagonist prior to the step of administering an anticholinesterase agent. It is respectfully submitted that the Examiner's rejection of claim 6 has been obviated.

In like manner, the applicants have amended claim 7 to read that the process further comprises the step of administering said anticholinesterase to said patient after said step of measuring said level of said anticholinesterase in said brain of said patient. Claims 3 and 5 clearly indicate the step of step of measuring the level of the anticholinesterase in the brain of the patient follows first administering the anticholinesterase in amended claim 1. Thus the step of claim 7 of administering the anticholinesterase to the patient after the step of measuring the level of the anticholinesterase in the brain of the patient is clearly distinct from the step of claim 1 of first administering the antagonist prior to the step of first administering an anticholinesterase agent. It is respectfully submitted that the Examiner's rejection of claim 7 has been obviated.

The Examiner has rejected claims 5 and 8 under 35 USC 112, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. The Examiner has indicated that the omitted steps are how the concentrations of the antagonist and anticholinesterase are determined in the patient's brain, what controls are

used, and what is measured in terms of units. The applicants have amended claim 5 to be directed to measuring said level of said antagonist in the brain of said patient, for which there is antecedent basis in claim 3. The applicants have amended claim 8 to be directed to measuring said level of said anticholinesterase in said brain of said patient, for which there is antecedent basis in claim 7. Bases for the measurement of such levels may be found at page 13, lines 1 – 16 of the specification. It is respectfully submitted that the Examiner's rejection of claim 5 and claim 8 has been obviated.

The Examiner has rejected claims 1 - 9 under 35 USC 103(a), as being unpatentable over United States patent 5,668,117 of Shapiro in view of United States patent 6,094,598 of Elsberry et al. It is first noted that the Examiner's rejection indicated in paragraph 13 therein, "...in view of US 5683422." However, in subsequent paragraphs 15 – 18, the Examiner's rejection is based upon being in view of United States patent 6,094,598 of Elsberry. Furthermore, the Examiner has noted in his Notice of References Cited attached to the Office Action of January 24, 2003 only the Shapiro and Elsberry references, and included copies of only such references. The applicants therefore infer that the Examiner's rejection is based upon the Shapiro and Elsberry references, and thus direct their remarks and arguments toward such references.

The Examiner has alleged that United States patent 5,668,117 of Shapiro teaches a process for treating Alzheimer's disease comprising administering two or more therapeutic agents, and further teaches, "a method of clinical treatment of Alzheimer's disease including the combination of a psychotherapeutic drug, such as haloperidol, and and acetylycholinesterase inhibitor, such as Cognex™."

The applicants have amended claim 1, adding the further limitation at line 6 thereof that "said antagonist of said neurotransmitter binds to and inhibits a neurotransmitter receptor, which leads to the ~~phosphorylates~~ phosphorylation of said microtubule-associated protein-2 in limbic cells" and the further limitation at lines 8 – 9 thereof that "said antagonist of said neurotransmitter binds to and inhibits a neurotransmitter receptor which leads to the ~~phosphorylates~~ phosphorylation of said microtuble-associated protein-2 in neocortical cells." Bases for this amendment may be found at page 8, paragraphs 3 and 4 of the specification, and in Figure 1.

The applicants respectfully submit that claim 1 as amended is not obvious in view of the cited references, noting in particular that the Shapiro invention (and the Examples cited thereof in United States patent 5,668,117) is to use, "at least one carbonyl trapping agent alone or in combination with a therapeutically effective of a co-agent or a medicament." The medicaments of the current invention are not carbonyl trapping agents. Hence there is no obvious overlap or similarity between Shapiro and the current invention.

Regarding the Examiner's assertion that the instant application discloses the same as the Shapiro reference with respect to combining haloperidol and an anticholinesterase, the applicants note that the drug haloperidol was only listed in way of an example in the instant patent application, and has been cancelled in the instant amendment. In addition, the used of haloperidol is actually excluded by the specification on page 7 of the instant application, where it is stated that:

"It is preferred that the candidate antagonist identified in steps 10 et seq. antagonizes functional activity in cholinoceptive cells relevant to cognition

preferentially in limbic brain regions (where neuropathology is concentrated) vs. neocortical sites. Such antagonist agents might include: muscarinic antagonists that act postsynaptically (i.e., M1, M3 and M5 subtypes) and, moreover, that preferentially antagonize cholinoceptive cells in limbic regions of the brain (i.e., hippocampus, parahippocampal gyrus, cingulate cortex and orbitofrontal cortex) **significantly more (i.e., at a ratio of 1.5 or greater)** than antagonize neocortical regions (i.e., primary, secondary and tertiary sensory cortices and association areas of the frontal, parietal, temporal and occipital lobes)."

And subsequently at page 12 it is stated that,

"For an antagonist to be useful in the process of this invention, it is preferred that **the ratio of its limbic cell effect to its neocortical cell effect be at least about 1.5**. In another embodiment, it is preferred that such ratio be at least about 2.5."

And in the Abstract (amended herein), it is stated,

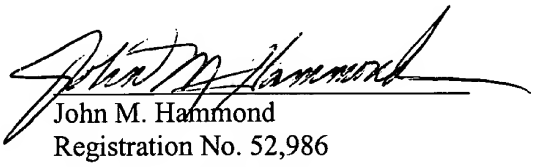
"A process for treating Alzheimer's disease, comprising the steps of administering to a human patient an antagonist of a neurotransmitter receptor which indirectly inhibits phosphorylation of microtubule-associated protein-2, and thereafter administering to the patient an anticholinesterase agent. The antagonist of the neurotransmitter binds to a neurotransmitter receptor which phosphorylates the microtubule-associated protein-2 in limbic cells, the antagonist of the neurotransmitter binds to a neurotransmitter receptor which phosphorylates microtuble-associated protein-2 in neocortical cells, and the antagonist binds to the neurotransmitter receptor in the limbic cells at least 1.5 times as much as it binds to the neurotransmitter receptor in the neocortical cells."

Thus it is respectfully submitted that nowhere in the Shapiro reference U.S. patent 5,668,117 and the Elsberry reference, U.S. patent 6,094,598, is there shown or suggested the process steps of claim 1 of the instant application, and that the Shapiro invention, being directed to the use of at least one carbonyl trapping agent alone or in combination with a therapeutically effective of a co-agent, in fact teaches away from the claimed invention. It is respectfully submitted that claim 1 as amended is therefore allowable. It is further respectfully submitted that claims 2 – 9 as amended, being dependent upon claim 1 which is allowable, are also now all allowable.

By the instant amendment, applicants have amended their case, thereby placing claim 1, and claims 2 – 9 dependent thereupon, in allowable form. Applicants have further amended the specification and submitted formal drawings in order to obviate the Examiner's objections thereto. It is respectfully submitted that with the instant amendment, the applicants' case is now allowable, and allowance thereof is respectfully requested. Applicants have also included a Petition for an Extension of Time for a period of 3 months, and check for $465.00 for payment of the fee for such an extension.

If for any reason the Examiner believes that a telephone conference might facilitate the prosecution of this case, he is respectfully requested to call Applicants' agent, John M. Hammond. In the event that any additional fees are due, please charge such fees to Deposit Account 50-2753.

Respectfully submitted,



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